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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,163	12/20/2001	Sanjay Lakhotia	AM100039	1674

25291 7590 01/25/2007  
WYETH  
PATENT LAW GROUP  
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EXAMINER

FORD, VANESSA L

ART UNIT PAPER NUMBER

1645

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/25/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

**Office Action Summary**

Application No.

10/019,163

Applicant(s)

LAKHOTIA ET AL.

Examiner

Vanessa L. Ford

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 27 October 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 December 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

**FINAL ACTION**

1. This Office Action is responsive to Applicant's amendment and response filed October 27, 2006.
2. The text of those sections of the Title 35, U.S. code not included in this action can be found in the prior Office Action.

***Rejection Withdrawn***

3. In view of Applicant's remarks the rejection under 35 U.S.C. 112, second paragraph page 2, paragraph 3 has been withdrawn.

***Rejection Maintained***

4. The rejection under 35 U.S.C. 103(a) is maintained for claims 1-16 for the reasons set forth on pages 3-4 paragraph 4 of the previous Office Action.

The rejection was on the grounds that Green et al teach a method of purifying bacteria using detergents such as Triton™ (column 4). Green et al teach that in a preferred embodiment the outer membrane components are prepared by differential solubilization of the inner membranes and outer membranes using Triton™ in HEPES-NaOH and MgCl<sub>2</sub> (Abstract and column 14). Green et al teach that a subfraction of the preparation of the outer membrane components which is rich in protein "e" (outer membrane protein P4 from *Haemophilus influenzae*) can be produced by extraction with an aqueous solution (column 4). Green et al teach that the protein "e" from the outer membrane cell wall complex can be then achieved by a two-step differential solubilization with sulfobetaine detergents (column 4). Green et al teach that the first step comprises an aqueous solution of Zwittergent™ to remove other outer membrane proteins other than protein "e" (column 4). Green et al teach that the residual insoluble components are then extracted with an aqueous solution of Zwittergent™ and this fraction results in the solubilization of protein "e"(column 4). Green et al teach that this process is performed in a homogenizer (column 14) since the instant specification teaches that a homogenizer is a microfluidizer (page 10 of the specification). Green et

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al teach that recombinant protein "e" can be isolated and purified by differential solubility (column 9).

Green et al do not teach tangential flow filtration (TFF).

Nicholson teaches a method of extracting recombinant proteins using tangential flow filtration (TFF) (column 10). Nicholson et al teaches that using their method is advantages because the proteins purified by the method have a high yield and was entirely homodimeric (see the Abstract).

It would be *prima facie* obvious at the time the invention was made to use tangential flow filtration as taught by Nicholson to extract bacterial proteins (inner and outer membrane) because Nicholson teaches that using TFF has the benefit of high yields and entirely homodimeric. It would be expected barring evidence to the contrary that using tangential flow filtration in a method of extracting proteins would offer high quality and high yield proteins.

#### Applicant's Arguments

Applicant urges that the Examiner ignores that the main points of Nicholson clearly states that "after removing cell" from the cell culture expressing human interleukin-5 (IL-5), IL5 is purified by first adjusting the culture supernatant to the calculated PI value of mature IL-5. Applicant urges that Nicholson is directed to methodologies that specifically allow the mammalian cells to remain intact and not be lysed where as the claimed invention specifically deals with the critical combination of lysed bacterial cells and tangential flow (TFF). Applicant urges that one skilled in the art would be motivated to avoid using TFF when dealing with a preparation of lysed bacterial cells. Applicant urges that is no direction to the benefits of TFF is given anywhere in Nicholson, nor is it in any way taught as being superior to any other method for the use described. Applicant urges that Nicholson teaches away from its use in the instance of the situation faced by the inventors of the claimed invention. Applicant urges that there is no teaching or suggestion that TFF be combined with the differential detergent extraction of Green et al to obtain the claimed invention.

Examiner's Response to Applicant's Amendments

Applicant arguments filed October 27, 2006 have been fully considered but they are not persuasive.

It is the Examiner's position that Applicant is arguing the references individually. It should be remembered that it is the combination of references that teaches the claimed invention.

In response to applicant's argument that there is no motivation to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the skilled artisan would be motivated to use tangential flow filtration as taught by Nicholson in the method of extracting proteins of Green et al because Nicholson tangential flow filtration (TFF) removes low molecular weight compounds. Nicholson et al teaches that using their method is advantageous because the proteins purified by the method have a high yield and was entirely homodimeric. Therefore, one of ordinary skill in the art would be motivated to use TFF in extraction methods to arrive at purified products.

The Examiner disagrees with Applicant's assertion that Nicholson teaches away from using lysed cells. As stated above it is the combination of references that teach

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the claimed invention. It should be noted that Nicholson is used to teach that after cell have been lysed, tangential flow filtration is used to remove low molecular weight components. Therefore, one of ordinary skill in the art would be motivated to use TFF in extraction methods to arrive at purified products. One of ordinary skilled in the art would have a reasonable expectation of success by combining the prior art references to arrive at the claimed invention.

In view of all of the above, there is nothing on the record to suggest that the combination of reference does not teach the claimed invention.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

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### **Status of Claims**

6. No claims allowed.

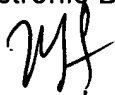
### **Conclusion**

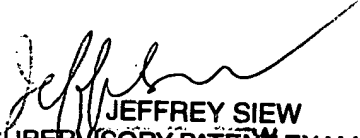
7. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (571) 273-8300.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffery Siew, can be reached at (571) 272-0787.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov./>>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Vanessa L. Ford  
Biotechnology Patent Examiner  
January 16, 2007

  
JEFFREY SIEW  
SUPERVISORY PATENT EXAMINER  
SUPERVISOR